```
FILE 'HOME' ENTERED AT 14:49:54 ON 01 OCT 2007
ENTER COST CENTER (NONE):none

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.42       0.42

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
       AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
       CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
       DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 14:50:53 ON 01 OCT 2007

69 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s
((N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-su
lphonamide) or (endothelin a receptor antagonist) or (ZD4054)) (p) (bisphosphonate
or pamidronic or zoldronic) (p) (prostate cancer)
MISSING OPERATOR 'N-(3-METHOXY-'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s
(N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sul
phonamide or (endothelin a receptor antagonist) or (ZD4054)) (p) (bisphosphonate or
pamidronic or zoldronic) (p) (prostate cancer)
MISSING OPERATOR 'N-(3-METHOXY-'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s ((N(1A)(3
(1A)methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulph
onamide) or (endothelin a receptor antagonist) or (ZD4054)) (p) (bisphosphonate or
pamidronic or zoldronic) (p) (prostate cancer)
MISSING OPERATOR AZIN-2-YL)-2-
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s ((N(1A)(3
(1A)methoxy(1A)5(1A)methylpyrazin(1A)2(1A)yl)(1A)2(1A)(4(1A)[1,3,4(1A)oxadiazol(1A)2
(1A)yl]phenyl)pyridine (1A)3 (1A)sulphonamide) or (endothelin a receptor
antagonist) or (ZD4054)) (p) (bisphosphonate or pamidronic or zoldronic) (p)
(prostate cancer)
MISSING OPERATOR YL]PHENYL)PYRIDINE
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s ((N(1A)(3
(1A)methoxy(1A)5(1A)methylpyrazin(1A)2(1A)yl)(1A)2(1A)(4(1A)[1,3,4(1A)oxadiazol(1A)2
(1A)yl]phenyl)(1A)pyridine (1A)3 (1A)sulphonamide) or (endothelin a receptor
antagonist) or (ZD4054)) (p) (bisphosphonate or pamidronic or zoldronic) (p)
(prostate cancer)
          0*  FILE ADISNEWS
          0*  FILE ANTE
          0*  FILE AQUALINE
          0*  FILE BIOENG
   9 FILES SEARCHED...
          2   FILE BIOSIS
```

```
          0*  FILE BIOTECHABS
          0*  FILE BIOTECHDS
          0*  FILE BIOTECHNO
  13 FILES SEARCHED...
          0*  FILE CEABA-VTB
          0*  FILE CIN
  21 FILES SEARCHED...
          1   FILE DDFU
  23 FILES SEARCHED...
          1   FILE DRUGU
          1   FILE EMBASE
          0*  FILE ESBIOBASE
  30 FILES SEARCHED...
          0*  FILE FOMAD
          0*  FILE FOREGE
          0*  FILE FROSTI
          0*  FILE FSTA
          1   FILE IFIPAT
  37 FILES SEARCHED...
          0*  FILE KOSMET
          0*  FILE NTIS
          0*  FILE NUTRACEUT
          0*  FILE PASCAL
  47 FILES SEARCHED...
          0*  FILE PHARMAML
          1   FILE PHIN
  56 FILES SEARCHED...
          2   FILE SCISEARCH
  61 FILES SEARCHED...
  63 FILES SEARCHED...
          0*  FILE WATER
  68 FILES SEARCHED...

   7 FILES HAVE ONE OR MORE ANSWERS,   69 FILES SEARCHED IN STNINDEX

L1   QUE ((N(1A)(3 (1A) METHOXY(1A) 5(1A) METHYLPYRAZIN(1A) 2(1A) YL)(1A) 2(1A)
         (4(1A) [1,3,4(1A) OXADIAZOL(1A) 2(1A) YL]PHENYL)(1A) PYRIDINE (1A) 3 (
         1A) SULPHONAMIDE) OR (ENDOTHELIN A RECEPTOR ANTAGONIST) OR (ZD4054)) (
         P) (BISPHOSPHONATE OR PAMIDRONIC OR ZOLDRONIC) (P) (PROSTATE CANCER)

=> s ((N(1A)(3
(1A)methoxy(1A)5(1A)methylpyrazin(1A)2(1A)yl)(1A)2(1A)(4(1A)[1,3,4(1A)oxadiazol(1A)2
(1A)yl]phenyl)(1A)pyridine (1A)3 (1A)sulphonamide) or (endothelin a receptor
antagonist) or (ZD4054)) and (bisphosphonate or pamidronic or zoldronic) and
(prostate cancer)
          1   FILE ADISCTI
          4   FILE BIOSIS
  11 FILES SEARCHED...
  13 FILES SEARCHED...
          1   FILE DDFU
  23 FILES SEARCHED...
          2   FILE DRUGU
          6   FILE EMBASE
  30 FILES SEARCHED...
          1   FILE IFIPAT
  43 FILES SEARCHED...
  47 FILES SEARCHED...
          1   FILE PHIC
          2   FILE PHIN
          2   FILE PROUSDDR
          2   FILE SCISEARCH
  60 FILES SEARCHED...
          5   FILE USPATFULL
  63 FILES SEARCHED...
```

11 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L2 QUE ((N(1A)(3 (1A) METHOXY(1A) 5(1A) METHYLPYRAZIN(1A) 2(1A) YL)(1A) 2(1A) (4(1A) [1,3,4(1A) OXADIAZOL(1A) 2(1A) YL]PHENYL)(1A) PYRIDINE (1A) 3 ( 1A) SULPHONAMIDE) OR (ENDOTHELIN A RECEPTOR ANTAGONIST) OR (ZD4054)) A ND (BISPHOSPHONATE OR PAMIDRONIC OR ZOLDRONIC) AND (PROSTATE CANCER)

=> file biosis, embase, scisearch, hcaplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 15.12 | 15.54 |

FILE 'BIOSIS' ENTERED AT 15:05:08 ON 01 OCT 2007
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FILE 'EMBASE' ENTERED AT 15:05:08 ON 01 OCT 2007
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FILE 'SCISEARCH' ENTERED AT 15:05:08 ON 01 OCT 2007
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FILE 'HCAPLUS' ENTERED AT 15:05:08 ON 01 OCT 2007
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> s l2
L3 12 L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 8 DUP REM L3 (4 DUPLICATES REMOVED)

=> d l4 1-8 ibib, kwic

L4 ANSWER 1 OF 8 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007069872 EMBASE
TITLE: Therapeutic options in advanced ***prostate cancer***: Present and future.
AUTHOR: Sowery R.D.; So A.I.; Gleave M.E.
CORPORATE SOURCE: Dr. M.E. Gleave, Prostate Centre, Vancouver General Hospital, 2775 Laurel Street, Vancouver, BC V5Z1M9, Canada. m.gleave@ubc.ca
SOURCE: Current Urology Reports, (Jan 2007) Vol. 8, No. 1, pp. 53-59.
Refs: 38
ISSN: 1527-2737 E-ISSN: 1534-6285
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Mar 2007
Last Updated on STN: 14 Mar 2007

TI Therapeutic options in advanced ***prostate cancer***: Present and future.

AB Patients with advanced ***prostate cancer*** now have many treatment options available including first- and second-line hormonal therapy, radiotherapy, ***bisphosphonate*** therapy with zoledronic

acid, and taxane-based chemotherapy. These options now give clinicians an opportunity to offer their patients symptomatic relief and most importantly improve overall survival. This article reviews the current treatment options available for men with advanced ***prostate cancer***. In addition, novel treatment options under development, including calcitriol, immunotherapies, small molecule inhibitors, and nucleotide-based targeted therapy, are discussed. Copyright. . .

CT Medical Descriptors:
advanced . . . side effect
jaw disease: SI, side effect
musculoskeletal disease: SI, side effect
myalgia: SI, side effect
nail disease: SI, side effect
neutropenia: SI, side effect
nucleotide sequence
****prostate cancer: DT, drug therapy***
****prostate cancer: RT, radiotherapy***
review
sensory neuropathy: SI, side effect
symptomatology
thromboembolism: SI, side effect
treatment outcome
aminoglutethimide: DT, drug therapy
antiandrogen: DT, drug therapy
atrasentan: DT, drug. . . EC, endogenous compound
cyproterone acetate: DT, drug therapy
dn 101
docetaxel: AE, adverse drug reaction
docetaxel: CT, clinical trial
docetaxel: CB, drug combination
docetaxel: DT, drug therapy
***endothelin A receptor antagonist: DT, drug therapy***
***endothelin A receptor antagonist: PD, pharmacology***
estramustine: AE, adverse drug reaction
estramustine: CB, drug combination
flutamide: DT, drug therapy
gonadorelin agonist: DT, drug therapy
gti 2501
hydrocortisone:. . .

L4 ANSWER 2 OF 8 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006256629 EMBASE
TITLE: New alternatives for the management of patients with hormone-refractory ***prostate cancer***.
AUTHOR: Nelson J.B.; Kantoff P.W.; Sartor A.O.; Petrylak D.P.
CORPORATE SOURCE: Dr. J.B. Nelson, Department of Urology, University of Pittsburgh School of Medicine, 5200 Center Avenue, Pittsburgh, PA 15232, United States. nelsonjb@msx.upmc.edu
SOURCE: Advanced Studies in Medicine, (Apr 2006) Vol. 6, No. 4 C, pp. S300-S312.
Refs: 48
ISSN: 1530-3004 CODEN: ASMDCT
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jun 2006
Last Updated on STN: 23 Jun 2006

TI New alternatives for the management of patients with hormone-refractory ***prostate cancer***.

AB Nearly all men receiving androgen deprivation therapy for metastatic ***prostate cancer*** will ultimately manifest evidence of disease progression, thus requiring a re-evaluation of treatment strategy. Treatment alternatives for men with hormone-refractory ***prostate cancer*** (HRPC) have been limited to palliative care in the absence of a survival advantage associated with chemotherapy. In 2004, docetaxel-based. . . HRPC, were shown to confer a significant survival advantage in 2 large, randomized, controlled phase III trials. Bone-targeted therapies, specifically ***endothelin-A receptor antagonists*** (eg, atrasentan), bone-targeted radiopharmaceuticals, and ***bisphosphonates*** (eg, zoledronic acid), directly address the bone-stromal interactions underlying painful bone metastases. Atrasentan potentially reduces the incidence of and delays. . .

CT Medical Descriptors:
bone . . . drug therapy
cancer immunotherapy
cancer survival
clinical trial
drug dose regimen
drug fatality: SI, side effect
drug mechanism
drug targeting
febrile neutropenia: SI, side effect
gastrointestinal symptom: SI, side effect
***hormone refractory prostate cancer: DM, disease management***
***hormone refractory prostate cancer: DT, drug therapy***
human
jaw disease: SI, side effect
male
neutropenia: SI, side effect
***prostate cancer: DM, disease management***
***prostate cancer: DT, drug therapy***
quality of life
review
sensory neuropathy: SI, side effect
thrombosis: DT, drug therapy
thrombosis: SI, side effect
treatment failure
treatment response
alkaline phosphatase:. . . adverse drug reaction
docetaxel: CT, clinical trial
docetaxel: CB, drug combination
docetaxel: CM, drug comparison
docetaxel: DO, drug dose
docetaxel: DT, drug therapy
endothelin 1
endothelin A receptor
***endothelin A receptor antagonist: CT, clinical trial***
***endothelin A receptor antagonist: DT, drug therapy***
***endothelin A receptor antagonist: PD, pharmacology***
estramustine: AE, adverse drug reaction
estramustine: CT, clinical trial
estramustine: CB, drug combination
estramustine: CM, drug comparison
estramustine: DO, drug. . .

L4 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
ACCESSION NUMBER: 2006:194368 BIOSIS
DOCUMENT NUMBER: PREV200600199056
TITLE: Combined ***bisphosphonate*** and ***endothelin***

***a receptor antagonist*** treatment
more effectively reduces ***prostate cancer***
growth in bone than either alone.

AUTHOR(S): Mohammad, K. S. [Reprint Author]; McKenna, C.; Mison, A.; Niewolna, M.; Vessella, R.; Corey, E.; Guise, T. A.

CORPORATE SOURCE: Univ Virginia, Charlottesville, VA USA

SOURCE: Journal of Bone and Mineral Research, (SEP 2005) Vol. 20, No. 9, Suppl. 1, pp. S54.
Meeting Info.: 27th Annual Meeting of the American-Society-for-Bone-and-Mineral-Research. Nashville, TN, USA. September 23 -27, 2005. Amer Soc Bone & Mineral Res.
CODEN: JBMREJ. ISSN: 0884-0431.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 22 Mar 2006
Last Updated on STN: 22 Mar 2006

TI Combined ***bisphosphonate*** and ***endothelin a receptor antagonist*** treatment more effectively reduces ***prostate cancer*** growth in bone than either alone.

IT . . .
of Organisms
serum: blood and lymphatics; bone: skeletal system; prostate: reproductive system; osteoclast: skeletal system; osteoblast: skeletal system

IT Diseases
***prostate cancer***: urologic disease, reproductive system disease/male, neoplastic disease
Prostatic Neoplasms (MeSH)

IT Diseases
osteoblastic bone metastasis: neoplastic disease, bone disease, drug therapy, . . .

IT Chemicals & Biochemicals
prostate specific antigen [EC 3.4.21.77]; atrasentan: antineoplastic-drug; endothelin A receptor; zoledronic acid: antineoplastic-drug; endothelin-1: secretion, stimulation; ***bisphosphonate*** antiresorptive drugs: antineoplastic-drug

L4 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 2

ACCESSION NUMBER: 2006:320718 BIOSIS

DOCUMENT NUMBER: PREV200600319323

TITLE: Combined ***bisphosphonate*** and ***endothelin A receptor antagonist*** treatment more effectively reduces ***prostate cancer*** growth in bone than either alone.

AUTHOR(S): Mohammad, K. S. [Reprint Author]; McKenna, C.; Mison, A.; Niewolna, M.; Vessella, R.; Corey, E.; Guise, T. A.

CORPORATE SOURCE: Univ Virginia, Dept Internal Med, Div Endocrinol and Metab, Charlottesville, VA USA

SOURCE: Journal of Bone and Mineral Research, (2005) Vol. 20, No. Suppl. 2, pp. P42.
Meeting Info.: 4th North American Symposium on Skeletal Complications of Malignancy. Bethesda, MD, USA. April 28 -30, 2005. NIH.
CODEN: JBMREJ. ISSN: 0884-0431.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 21 Jun 2006
Last Updated on STN: 21 Jun 2006

TI Combined ***bisphosphonate*** and ***endothelin A receptor antagonist*** treatment more effectively reduces

***prostate cancer*** growth in bone than either alone.

IT . . .
(Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
plasma: blood and lymphatics; bone: skeletal system
IT Diseases
***prostate cancer***: urologic disease, reproductive system disease/male, neoplastic disease, drug therapy
Prostatic Neoplasms (MeSH)
IT Chemicals & Biochemicals
atrasentan: antineoplastic-drug, combination therapy; zoledronic. . .

L4 ANSWER 5 OF 8 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005224960 EMBASE
TITLE: Future therapies in hormone-refractory ***prostate cancer***.
AUTHOR: Smith M.R.; Nelson J.B.; DiPaola R.S.; Carducci M.A.; Thompson I.M.
CORPORATE SOURCE: Dr. J.B. Nelson, Univ. of Pittsburgh Medical Center, Department of Urology, Shadyside Medical Building, 5200 Centre Avenue, Pittsburgh, PA 15232, United States. nelsonjb@msx.upmc.edu
SOURCE: Urology, (May 2005) Vol. 65, No. 5 SUPPL., pp. 9-17. ISSN: 0090-4295 CODEN: URGYAZ
PUBLISHER IDENT.: S 0090-4295(05)00355-9
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jun 2005
Last Updated on STN: 16 Jun 2005

TI Future therapies in hormone-refractory ***prostate cancer***

AB Hormone-refractory ***prostate cancer*** (HRPC) remains true to its name: it is largely refractory to attempts to delay its progression. Although the number of men presenting with metastatic ***prostate cancer*** has decreased significantly over the last several years, the death rate for those men is essentially unchanged. To alter the. . .

CT Medical Descriptors:
adoptive . . . myeloid leukemia
clinical trial
conference paper
diarrhea: SI, side effect
disease activity
drug efficacy
drug indication
drug targeting
fatigue: SI, side effect
gynecomastia: SI, side effect
headache: SI, side effect
hormonal therapy
***hormone refractory prostate cancer: DT, drug therapy***
human
hypercalcemia: DT, drug therapy
hypercalcemia: PC, prevention
hypercalcemia: SI, side effect
hypertension: SI, side effect
hypotension: SI, side effect

hypothalamus. . . gonad system
kidney dysfunction: SI, side effect
lung non small cell cancer
neurotoxicity: SI, side effect
osteoclast
phocomelia: SI, side effect
postmenopause osteoporosis: DT, drug therapy
priority journal
***prostate cancer: DT, drug therapy***
thromboembolism: SI, side effect
abarelix: CT, clinical trial
abarelix: DT, drug therapy
abarelix: PD, pharmacology
androgen: EC, endogenous compound
angiogenesis inhibitor:. . . adverse drug reaction
diethylstilbestrol: DT, drug therapy
docetaxel: AE, adverse drug reaction
docetaxel: CB, drug combination
docetaxel: CM, drug comparison
docetaxel: DT, drug therapy
docetaxel: PD, pharmacology
***endothelin A receptor antagonist: AE, adverse drug reaction***
***endothelin A receptor antagonist: CT, clinical trial***
***endothelin A receptor antagonist: CB, drug combination***
***endothelin A receptor antagonist: DO, drug dose***
***endothelin A receptor antagonist: DT, drug therapy***
***endothelin A receptor antagonist: PD, pharmacology***
erlotinib: CT, clinical trial
erlotinib: DT, drug therapy
gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
gonadorelin antagonist:. . . DT, drug therapy
mitoxantrone: CT, clinical trial
mitoxantrone: CB, drug combination
mitoxantrone: DT, drug therapy
mitoxantrone: PD, pharmacology
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
***pamidronic acid: CT, clinical trial***
***pamidronic acid: CM, drug comparison***
***pamidronic acid: DT, drug therapy***
***pamidronic acid: IV, intravenous drug administration***
***pamidronic acid: PD, pharmacology***
panitumumab: CT, clinical trial
panitumumab: DT, drug therapy
pc spes: AE, adverse drug reaction
pc spes: CT, clinical trial
pc spes: PD,. . .
RN. . . 56-53-1; (docetaxel) 114977-28-5; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (ketoconazole) 65277-42-1; (leflunomide) 75706-12-6; (mitoxantrone) 65271-80-9, 70476-82-3; (***pamidronic*** acid) 40391-99-9, 57248-88-1; (panitumumab) 339177-26-3; (prednisone) 53-03-2; (rituximab) 174722-31-7; (thalidomide) 50-35-1; (tipifarnib) 192185-72-1; (trastuzumab) 180288-69-1; (zoledronic acid) 118072-93-8, 131654-46-1, 165800-06-6,. . .

L4 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 3
ACCESSION NUMBER: 2003:389985 BIOSIS
DOCUMENT NUMBER: PREV200300389985
TITLE: Treatments for improving survival of patients with ***prostate cancer***.

AUTHOR(S): David, Alice K.; Khwaja, Radhika; Hudes, Gary R. [Reprint Author]
CORPORATE SOURCE: Department of Medical Oncology, Fox Chase Cancer Center, 7701 Burholme Avenue, Philadelphia, PA, 19111, USA
g_hudes@fccc.edu
SOURCE: Drugs & Aging, (2003) Vol. 20, No. 9, pp. 683-699. print.
ISSN: 1170-229X (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Aug 2003
Last Updated on STN: 18 Sep 2003

TI Treatments for improving survival of patients with ***prostate cancer***.

IT . . .
disease, neoplastic disease, therapy
Bone Neoplasms (MeSH); Neoplasm Metastasis (MeSH)

IT Diseases
metastatic disease: neoplastic disease, therapy
Neoplasm Metastasis (MeSH)

IT Diseases
***prostate cancer***: neoplastic disease, reproductive system disease/male, urologic disease, pathology, therapy
Prostatic Neoplasms (MeSH)

IT Chemicals & Biochemicals
atrasentan: antineoplastic-drug, ***endothelin-A receptor antagonist***; ***bisphosphonates***: antineoplastic-drug; endothelin-A receptor; prostate specific antigen [EC 3.4.21.77]: tumor marker; radionuclides: antineoplastic-drug; radiopharmaceuticals: antineoplastic-drug; receptor tyrosine kinase inhibitors: antineoplastic-drug, enzyme. . .

RN 173937-91-2 (atrasentan)
13598-36-2 (***bisphosphonates***)

L4 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 4
ACCESSION NUMBER: 2003:206977 BIOSIS
DOCUMENT NUMBER: PREV200300206977
TITLE: Endothelin and skeletal metastases in hormone-refractory ***prostate cancer***.
AUTHOR(S): Hamdy, Freddie C. [Reprint Author]
CORPORATE SOURCE: Academic Urology Unit, Division of Clinical Sciences, Royal Hallamshire Hospital, University of Sheffield, Sheffield, UK
f.c.hamdy@sheffield.ac.uk
SOURCE: European Urology Supplements, (March 2003) Vol. 2, No. 3, pp. 15-19. print.
ISSN: 1569-9056 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Apr 2003
Last Updated on STN: 23 Apr 2003

TI Endothelin and skeletal metastases in hormone-refractory ***prostate cancer***.

AB Skeletal metastases represent a major complication of advanced hormone-refractory ***prostate cancer*** (HRPC). These lesions affect around 85% of patients and provide a poor quality of life due to associated pathological fractures,. . . diagnosis. At present, there is no effective treatment for delaying disease progression. Current treatment options based on chemotherapy, radiotherapy and ***bisphosphonates*** are essentially palliative and do not appear to prolong survival. HRPC, therefore, represents a considerable unmet clinical need, and new. . .

IT . . .

Pharmacology; Urology (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
bone: skeletal system, remodeling; osteoblast: skeletal system; ***prostate cancer*** cell: excretory system, reproductive system
IT Diseases
metastatic hormone-refractory ***prostate cancer***: neoplastic disease, reproductive system disease/male, urologic disease, drug therapy
IT Diseases
skeletal metastatic disease: bone disease, neoplastic disease, drug therapy
IT Chemicals & Biochemicals
endothelin-1: therapeutic target; ***endothelin-A receptor antagonist***: antineoplastic-drug

L4 ANSWER 8 OF 8 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003402002 EMBASE
TITLE: Skeletal complications of malignancy - Third North American Symposium: 25-27 April 2002, Bethesda, MD, USA.
AUTHOR: Bagi C.
CORPORATE SOURCE: C. Bagi, Pfizer Inc., Groton Laboratories, Eastern Point Road 8118E/3, Groton, CT 06340, United States. cedo_bagi@groton.pfizer.com
SOURCE: IDrugs, (2002) Vol. 5, No. 6, pp. 553-556.
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
030 Clinical and Experimental Pharmacology
029 Clinical and Experimental Biochemistry
017 Public Health, Social Medicine and Epidemiology
016 Cancer
014 Radiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 Oct 2003
Last Updated on STN: 23 Oct 2003

AB . . . diagnostic tools, and effective anticancer therapy. In addition, life expectancy is prolonged, in particular those patients suffering from breast and ***prostate cancer***. Bone metastases are a frequent event in a variety of cancer types. Dissemination of the carcinomas of the breast and. . .

CT Medical Descriptors:
aging
bone . . . disease: DM, disease management
*malignant neoplastic disease: DT, drug therapy
*malignant neoplastic disease: RT, radiotherapy
multiple myeloma: DR, drug resistance
multiple myeloma: DT, drug therapy
nonhuman
osteolysis
osteoporosis
prevalence
***prostate cancer: DT, drug therapy***
quality of life
side effect: SI, side effect
single drug dose
stroma
thyroid cancer
treatment failure
amgn 0007: CM, drug comparison

amgn 0007:. . . DT, drug therapy
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
endothelin 1: EC, endogenous compound
endothelin A receptor: EC, endogenous compound
***endothelin A receptor antagonist: PD, pharmacology***
etidronic acid: AN, drug analysis
etidronic acid: PK, pharmacokinetics
fluorouracil: CB, drug combination
fluorouracil: CM, drug comparison
fluorouracil: DT, drug. . . drug analysis
ibandronic acid: PK, pharmacokinetics
immunomodulating agent: PD, pharmacology
methotrexate: CB, drug combination
methotrexate: CM, drug comparison
methotrexate: DT, drug therapy
neurotrophin receptor: EC, endogenous compound
***pamidronic acid: CT, clinical trial***
***pamidronic acid: AN, drug analysis***
***pamidronic acid: CB, drug combination***
***pamidronic acid: CM, drug comparison***
***pamidronic acid: DT, drug therapy***
***pamidronic acid: IV, intravenous drug administration***
***pamidronic acid: PD, pharmacology***
parathyroid hormone related protein monoclonal antibody: DT, drug therapy
parathyroid hormone related protein monoclonal antibody: IV, intravenous drug administration
selective. . .
RN. . . (doxorubicin) 23214-92-8, 25316-40-9; (etidronic acid) 2809-21-4, 3794-83-0, 58449-82-4, 7414-83-7; (fluorouracil) 51-21-8; (ibandronic acid) 114084-78-5, 138844-81-2, 138926-19-9; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (***pamidronic*** acid) 40391-99-9, 57248-88-1; (strontium 89) 14158-27-1; (tamoxifen) 10540-29-1; (thalidomide) 50-35-1; (zoledronic acid) 118072-93-8, 131654-46-1, 165800-06-6, 165800-07-7

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AB Patients with advanced ***prostate cancer*** now have many treatment options available including first- and second-line hormonal therapy, radiotherapy, ***bisphosphonate*** therapy with zoledronic acid, and taxane-based chemotherapy. These options now give clinicians an opportunity to offer their patients symptomatic relief and most importantly improve overall survival. This article reviews the current treatment options available for men with advanced ***prostate cancer***. In addition, novel treatment options under development, including calcitriol, immunotherapies, small molecule inhibitors, and nucleotide-based targeted therapy, are discussed. Copyright .COPYRGT. 2007 by Current Medicine Group LLC.

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AB Nearly all men receiving androgen deprivation therapy for metastatic ***prostate cancer*** will ultimately manifest evidence of disease progression, thus requiring a re-evaluation of treatment strategy. Treatment alternatives for men with hormone-refractory ***prostate cancer*** (HRPC) have been limited to palliative care in the absence of a survival advantage associated with chemotherapy. In 2004, docetaxel-based chemotherapeutic regimens, now the standard for HRPC, were shown to confer a significant survival advantage in 2 large, randomized, controlled phase III trials. Bone-targeted therapies, specifically

***endothelin-A receptor antagonists*** (eg, atrasentan), bone-targeted radiopharmaceuticals, and ***bisphosphonates*** (eg, zoledronic acid), directly address the bone-stromal interactions underlying painful bone metastases. Atrasentan potentially reduces the incidence of and delays time to the onset of bone pain, may delay time to disease progression, and may improve the quality of life in patients with HRPC. Zoledronic acid was shown, in a phase III trial, to decrease the incidence of skeletal-related events and prolong the time to a first skeletal-related event in men with HRPC. Bone-targeted radiopharmaceuticals have been shown in phase III trials to decrease bone pain and decrease opioid utilization in patients with bony metastatic disease. Clinical trials are in progress to identify novel agents, in addition to optimize the combination of chemotherapeutic, bone-targeted agents and immunologic approaches. A wide variety of novel approaches, including immunologic therapies, are being tested.

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L4 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
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AB Hormone-refractory ***prostate cancer*** (HRPC) remains true to its name: it is largely refractory to attempts to delay its progression. Although the number of men presenting with metastatic ***prostate cancer*** has decreased significantly over the last several years, the death rate for those men is essentially unchanged. To alter the currently inevitable progression of HRPC to death, new targets and new therapies are needed. This article reviews investigational therapies directed against standard targets (eg, the hypothalamic-pituitary-gonadal axis) as well as novel targets (eg, the endothelin axis). .COPYRGT. 2005 Elsevier Inc.

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DUPLICATE 4

AB Skeletal metastases represent a major complication of advanced hormone-refractory ***prostate cancer*** (HRPC). These lesions affect around 85% of patients and provide a poor quality of life due to associated pathological fractures, spinal compression and pain. Metastatic HRPC is incurable and typically fatal within 2 years of diagnosis. At present, there is no effective treatment for delaying disease progression. Current treatment options based on chemotherapy, radiotherapy and ***bisphosphonates*** are essentially palliative and do not appear to prolong survival. HRPC, therefore, represents a considerable unmet clinical need, and new therapies are required to alter the course of the disease process beyond providing palliation. Many factors are involved in bone remodelling, and a substantial body of evidence suggests a major role for endothelin-1 (ET-1) in the pathophysiology of bone lesions in metastatic HRPC. In HRPC, the binding of ET-1 to a specific receptor (ETA) not only enhances osteoblastic activity and promotes the development of metastatic bone lesions, but also generates a mitogenic and anti-apoptotic milieu. In vivo and in vitro studies show that ET-1-stimulated bone growth is inhibited when the ET-1 receptor (ETA) is blocked. Highly potent and specific ETA-receptor antagonists, therefore, represent an exciting development in the management of HRPC, providing a potentially effective therapeutic target for the delay or prevention of skeletal metastatic progression.

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AB Interest in the skeletal complications of malignancy continues to increase rapidly. There are several reasons for this growing trend including an aging population and higher incidence of cancer, improved diagnostic tools, and effective anticancer therapy. In addition, life expectancy is prolonged, in particular those patients suffering from breast and ***prostate cancer***. Bone metastases are a frequent event in a variety of cancer types. Dissemination of the carcinomas of the breast and prostate to the skeleton is particularly prevalent and also a notable feature of malignancy originating in the lungs, thyroid and kidneys. Multiple myeloma is a unique neoplastic disorder associated with extensive bone involvement. Important clinical problems that arise from cancer metastases to bone include humoral hypercalcemia of malignancy, cancer-associated osteoporosis and significant implications on the quality of life of cancer patients including bone pain. The major topic of the conference was treatment modalities targeting the prevention of skeletal disease. One particular focus was given to stromal-derived cytokines and growth factors due to evidence which indicates the critical role that bone marrow and stroma play in homing of tumors to the bone and development of bone metastases. .COPYRGT. PharmaPress Ltd.

| | Ref # | Hits | Search Text |
|---|---|---|---|
| 1 | S1 | 1 | ("2003092757").PN. |
| 2 | S2 | 3 | singh-amitabh.in. |
| 3 | S3 | 26091633 | N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide |
| 4 | S4 | 3610 | bisphosphonate |
| 5 | S5 | 1242 | lhrh adj analogue |
| 6 | S6 | 71 | bisphosphonate and lhrh adj analogue |
| 7 | S7 | 252 | bisphosphonate and goserelin |
| 8 | S8 | 12 | bisphosphonate and lhrh adj antagonist |
| 9 | S9 | 3 | "20030092757" |
| 10 | S10 | 82 | "5464853" |
| 11 | S11 | 71 | "5514691" |
| 12 | S12 | 9 | "5843902" |
| 13 | S13 | 36 | "5763429" |
| 14 | S14 | 119 | "4100274" |
| 15 | S15 | 316 | "4767628" |
| 16 | S16 | 2 | "20020055457" |
| 17 | S18 | 9 | (("5464853") or ("5514691") or ("5843902") or ("5763429") or ("4100274") or ("4767628") or ("20020055457") or ("20050014769")).PN. |
| 18 | S19 | 1 | ("5763429").PN. |
| 19 | S20 | 26443097 | N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide and bisphosphonate |
| 20 | S21 | 1 | ("20060009512").PN. |
| 21 | S22 | 1 | ("20060287241").PN. |
| 22 | S23 | 3 | ZD4054 |
| 23 | S24 | 1 | endothlin adj receptor adj antagonist |
| 24 | S25 | 0 | endothlin adj S9 adj antagonist |
| 25 | S26 | 0 | endothlin adj "1" adj antagonist |
| 26 | S27 | 26443097 | N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide and bisphosphonate and zd4054 |
| 27 | S28 | 1157 | endothelin adj receptor adj antagonist |
| 28 | S30 | 2 | endothelin adj receptor adj antagonist and ZD4054 |

| | Ref # | Hits | Search Text |
|---|---|---|---|
| 29 | S29 | 164 | endothelin adj receptor adj antagonist and bisphosphonate |
| 30 | S31 | 2 | "20050014769" |
| 31 | S32 | 19 | (("5292740") or ("5334598") or ("5378715") or ("5389620") or ("5420123") or ("5464853") or ("5482960") or ("5514691") or ("5514696") or ("5541186") or ("5543521") or ("5559105") or ("5571821") or ("5780473") or ("5962490") or ("5965732") or ("6080774") or ("6420567") or ("20020091272")).PN. |
| 32 | S33 | 83 | endothelin adj receptor adj antagonist and ((pamidronic adj acid) or pamidronate) |
| 33 | S34 | 1 | ("5866568").PN. |
| 34 | S35 | 13641 | carbamic adj acid |
| 35 | S36 | 280 | S35 and bisphosphonate |
| 36 | S38 | 134 | S36 and pamidronate |
| 37 | S37 | 56 | S36 and pamidronic adj acid |
| 38 | S39 | 344 | sulfonamide and pamidronic adj acid |
| 39 | S40 | 0 | sulfonamide and (endothelin adj receptor adj antagonist) and pamidronic adj acid |
| 40 | S41 | 1 | sulfonamide and (endothelin adj antagonist) and pamidronic adj acid |
| 41 | S42 | 0 | N "3" methoxy "5" methylpyrazin "2" yl "2" "4" "1" "3" "4" oxadiazol "2" yl phenyl pyridine "3" sulfonamide |
| 42 | S43 | 0 | N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide |
| 43 | S44 | 26443097 | N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide and bisphosphonate |
| 44 | S45 | 11321349 | endothelin adj receptor adj antagonist (s) bisphosphonate |
| 45 | S46 | 5490550 | endothelin adj receptor adj antagonist (p) bisphosphonate |
| 46 | S47 | 1 | ("4784684").PN. |

| | Ref # | Hits | Search Text |
|---|---|---|---|
| 47 | S48 | 5489796 | endothelin adj receptor adj antagonist (p) bisphosphonate and pamidronic adj acid |
| 48 | S49 | 2 | (("6060475") or ("6258817")).PN. |
| 49 | S50 | 1 | ("5866568").PN. |
| 50 | S51 | 5489791 | endothelin adj receptor adj antagonist (p) bisphosphonate and pamidronic adj acid and cancer |
| 51 | S52 | 2353 | bisphosphonate and cancer |
| 52 | S53 | 1582 | S52 and pamidronic adj acid or pamidronate |
| 53 | S54 | 83 | S53 and endothelin adj receptor adj antagonist |
| 54 | S55 | 550 | pamidronic adj acid |
| 55 | S56 | 272 | S55 and bisphosphonate |
| 56 | S57 | 551 | S53 and endothelin adj receptor adj antagonist and diphosphonate or biphosphonate |
| 57 | S58 | 60 | S53 and endothelin adj receptor adj antagonist and (diphosphonate or biphosphonate) |
| 58 | S59 | 60 | S53 and (endothelin adj receptor adj antagonist) and (diphosphonate or biphosphonate) |
| 59 | S60 | 166 | (endothelin adj receptor adj antagonist) and (diphosphonate or biphosphonate or bisphosphonate) |
| 60 | S61 | 0 | pyrazinyl adj oxadiazolyl adj pyridine adj sulfonamide adj endothelin adj receptor |
| 61 | S62 | 1 | ("20040259876").PN. |
| 62 | S63 | 1 | ("20060094729").PN. |
| 63 | S64 | 2353 | bisphosphonate and cancer |
| 64 | S65 | 778 | bisphosphonate and prostate adj cancer |
| 65 | S66 | 670 | bisphosphonate and prostate adj cancer and breast adj cancer |
| 66 | S67 | 136 | bisphosphonate and prostate adj cancer and breast adj cancer and bone adj metastasis |
| 67 | S68 | 42 | endothelin adj a adj receptor and prostate adj cancer |
| 68 | S69 | 21 | (endothelin adj a adj receptor adj antagonist) and prostate adj cancer |

| | Ref # | Hits | Search Text |
|---|---|---|---|
| 69 | S70 | 670 | bisphosphonate and prostate adj cancer and breast adj cancer |
| 70 | S71 | 41 | bisphosphonate and prostate adj cancer and breast adj cancer and (endothelin adj receptor adj antagonist) |
| 71 | S72 | 0 | zibotentan |
| 72 | S73 | 2 | ("2005115454").PN. |
| 73 | S74 | 1 | ("20050115454").PN. |
| 74 | S75 | 0 | ("2004569131").PN. |
| 75 | S76 | 0 | ("20040569131").PN. |
| 76 | S77 | 25 | zd4054 or bms247550 or kos862 or bms275291 |
| 77 | S78 | 4 | (zd4054 or bms247550 or kos862 or bms275291) and bisphosphonate |
| 78 | S79 | 285 | (zd4054 or bms247550 or kos862 or bms275291 or azd2171 or zd6474 or azd9935 or azd4440 or azd0530 or azd0424 or azd3409 or azd5438 or azd6244 or azd1152) |
| 79 | S80 | 81 | (zd4054 or bms247550 or kos862 or bms275291 or azd2171 or zd6474 or azd9935 or azd4440 or azd0530 or azd0424 or azd3409 or azd5438 or azd6244 or azd1152) and bisphosphonate |
| 80 | S81 | 81 | (zd4054 or bms247550 or kos862 or bms275291 or azd2171 or zd6474 or azd9935 or azd4440 or azd0530 or azd0424 or azd3409 or azd5438 or azd6244 or azd1152 or promune) and bisphosphonate |
| 81 | S82 | 1 | ("6258817").PN. |
| 82 | S83 | 1 | ("5866568").PN. |
| 83 | S84 | 1 | ("6060475").PN. |
| 84 | S85 | 0 | ("20030516192").PN. |
| 85 | S86 | 1 | ("20050148535").PN. |
| 86 | S87 | 1 | ("20060094729").PN. |
| 87 | S88 | 1 | ("20060122180").PN. |
| 88 | S89 | 1 | ("20060094729").PN. |
| 89 | S90 | 1 | ("20060009512").PN. |
| 90 | S91 | 1 | ("20060287241").PN. |

| | Ref # | Hits | Search Text |
|---|---|---|---|
| 91 | S92 | 41 | (zd4054 or bms247550 or kos862 or bms275291 or azd2171 or zd6474 or azd9935 or azd4440 or azd0530 or azd0424 or azd3409 or azd5438 or azd6244 or azd1152 or promune) and (pamidronate or (pamidronic adj acid)) |
| 92 | S93 | 11321349 | (endothelin adj receptor adj antagonist) (s) bisphosphonate |
| 93 | S94 | 5490550 | (endothelin adj receptor adj antagonist) (p) bisphosphonate |
| 94 | S96 | 11321086 | (endothelin adj receptor adj antagonist) (s) bisphosphonate.ab. |
| 95 | S97 | 5490211 | (endothelin adj receptor adj antagonist) (p) bisphosphonate.ab. |
| 96 | S98 | 5489984 | (endothelin adj receptor adj antagonist) (p) bisphosphonate.bsum. |
| 97 | S95 | 164 | (endothelin adj receptor adj antagonist) and bisphosphonate |
| 98 | S99 | 5510890 | (endothelin adj receptor adj antagonist) (p) bisphosphonate (p) cancer.bsum. |
| 99 | S100 | 50 | (endothelin adj receptor adj antagonist) and bisphosphonate and cancer.bsum. |
| 100 | S101 | 8 | (endothelin adj receptor adj antagonist) and bisphosphonate and cancer.ab. |
| 101 | S102 | 1 | ("20060287241").PN. |
| 102 | S103 | 1 | ("20020055457").PN. |
| 103 | S104 | 1 | ("20020055457").PN. |
| 104 | S105 | 3 | Gallagher-neil.in. |
| 105 | S106 | 27473442 | ZD4054 or (N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide) |
| 106 | S108 | 0 | (ZD4054 or (N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide) or (endothelin A receptor antagonist)) same bisphosphonate |

| | Ref # | Hits | Search Text |
|---|---|---|---|
| 107 | S109 | 10 | (ZD4054 or (N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide) or (endothelin A receptor antagonist)) and bisphosphonate |
| 108 | S110 | 10 | (ZD4054 or (N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide) or (endothelin A receptor antagonist)) and (bisphosphonate or pamidronic or zoldronic) |
| 109 | S111 | 10 | (ZD4054 or (N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide) or (endothelin A receptor antagonist)) and (bisphosphonate or pamidronic or zoldronic) |
| 110 | S112 | 0 | (endothelian receptor antagonist) same bisphosphonate |
| 111 | S113 | 144 | (endothelin receptor antagonist) same bisphosphonate |
| 112 | S114 | 0 | (endothelin receptor antagonist) same bisphosphonate same prostate cancer |
| 113 | S115 | 38 | (endothelin receptor antagonist) same bisphosphonate and prostate cancer |
| 114 | S116 | 38 | (endothelin receptor antagonist) same bisphosphonate and (prostate cancer) |
| 115 | S117 | 0 | (N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide) |